Patent
Attorney's Docket No. 033315-002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	)	
	)	
Christer NORDSTEDT et al.	)	
	)	Group Art Unit: Unassigned
Application No.: Unassigned	)	
	)	Examiner: Unassigned
Filed: May 8, 2001	)	
	)	
For: PEPTIDE BINDING KLVFF-SEQUENCE OF AMYLOID BETA	)	

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination of the above-captioned patent application, kindly enter the following amendment.

IN THE SPECIFICATION:

Kindly replace the Paragraph Beginning at Page 1, Line 2 with the following:

--This application is a divisional of U.S. Application No. 09/095,106, filed on June 10, 1998 which is a continuation of International Application No. PCT/SE96/01621, filed December 9, 1996, which International Application was published by the International Bureau in English on June 19, 1997, that designates the United States and which claims priority from Swedish Application No. 9504467-3, filed December 12, 1995, and U.S. Provisional Application No. 60/009,386, filed December 29, 1995, which are herein incorporated by reference.--

In compliance with 37 C.F.R. § 1.823(a), please insert the attached paper copy of the "Sequence Listing" (pages 1-8), after the last page of the above-identified application (page 22).

Kindly replace the Paragraph Beginning at Page 3, Line 32 with the following:

--According to the invention, it has now been found that the Lys-Leu-Val-Phe-Phe (KLVFF) sequence [SEQ ID NO.: 1] in Aß is necessary for polymerization to occur. Peptides incorporating this sequence bind to Aß and are capable of blocking the fibril formation of Aß-1-40 and are therefore potentially useful as drugs.--

Kindly replace the Paragraph Beginning at Page 9, Line 18 with the following:

--Fig. 2B. [SEQ ID NOS.: 1, 2 and 5-38] EVHHQKLVFF and N and C-terminal truncated fragments were synthesized and analyzed for affinity to ^{125}I-labeled Aß-1-40.--

Kindly replace the Paragraph Beginning at Page 9, Line 21 with the following:

--Fig. 2C. [SEQ ID NOS.: 39-43] Each amino acid residue in KLVFF was systematically replaced with Ala and analyzed for affinity to ^{125}I-labeled Aß-1-40.--

Kindly replace the Paragraph Beginning at Page 9, Line 24 with the following:

--Fig. 2D. [SEQ ID NO.: 44] Sensorgram from surface plasmon resonance spectroscopy (BIAcore 2000).--

Kindly replace the Paragraph Beginning at Page 12, Line 5 with the following:

--To investigate if the KLXXF [SEQ ID NO.: 3] motif was required for Aß polymerization, we synthesized Aß-1-28, a well-studied Aß fragment that readily forms amyloid fibrils (D.A. Kirschner, *et al., Proc. Natl. Acad. Sci.* USA 84, 6953-6957 (1987); C.J. Barrow, M.G. Zagorski, *Science* 253, 179-82 (1997); C. Nordstedt, *et al., J. Biol. Chem.* 269, 30773-30776 (1994))) and mutated Aß-1-28 where the KLVFF sequence was substituted with AAVFA [SEQ ID NO. 4] (Aß-1-28^{AAVFA}).--

IN THE CLAIMS:

Kindly add new claims 27-37 as follows:

27. (New) A method for inhibiting the polymerization of an amyloid β peptide to a ligand comprising contacting an amyloid β peptide containing environment with a polymerization inhibitory effective amount of a compound according to Claim 1.

28. (New) A method for inhibiting the polymerization of an amyloid β peptide comprising contacting an amyloid β peptide containing environment with a polymerization inhibiting effective amount of a compound according to Claim 1.

29. (New) A method for identifying an organic compound capable of inhibiting the polymerization of amyloid β peptide-ligands or for inhibiting the polymerization of amyloid β peptides based on the ability of such compound to affect the inhibition of polymerization of amyloid β peptide-ligands or the inhibition of polymerization of amyloid β peptides by a compound according to Claim 1.

30. (New) A method of screening a compound library for a compound capable of inhibiting the polymerization of amyloid β peptide-ligands or inhibiting the polymerization of amyloid β peptides based on the ability of such compound to bind to an amyloid β polypeptide in the region of the polypeptide comprising residues 16-20.

31. (New) A method for detecting amyloid deposits by positron emission tomography (PET), comprising detecting said deposit using as the ligand a compound according to Claim 1.

32. (New) A method of inhibiting the polymerization of amyloid β peptide-ligand or amyloid β peptide polymerization in a subject in need of such treatment comprising administering a therapeutic effective amount of a compound according to Claim 1.

33. (New) A method according to Claim 32, which is used to treat Alzheimer's disease or another disease characterized by amyloidoses.

34. (New) The method according to Claim 27 wherein the amino acids of the compound are all D-isomers.

35. (New) A method for treating or preventing demens in patients having Downs syndrome comprising administering an effective amount of a compound according to Claim 1.

36. (New) A method for treating or preventing hereditary cerebral hemorrhage associated with amyloidosis (Dutch type) comprising administering an effective amount of a compound according to Claim 1.

37. (New) A method for preventing fibral formation of human amyloid protein in a patient in need of such prevention comprising administering an effective amount of a compound according to Claim 1.

Remarks

Entry of the foregoing amendments, prior to examination, is respectfully requested. By this amendment, the paper copy of the "Sequence Listing" is added after the last page of the application (page 22), and claims 27-37 have been added. New claims 27-37 are supported by at least claims 11-24 as originally filed. No prohibited new matter has been added with these amendments.

Based on the foregoing, favorable examination on the merits is respectfully requested. If the Examiner has any specific questions relating to this Amendment or any other matter, he is respectfully requested to contact the undersigned so that prosecution of this application may be expedited.

Respectfully submitted,

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Attachment to Preliminary Amendment dated May 8, 2001

Marked-up Copy

Page 1, Paragraph Beginning at Line 2

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